

# Molecular dynamics study on water confinement in deep eutectic solvents



Alberto Gutiérrez<sup>a</sup>, Mert Atilhan<sup>b,\*</sup>, Santiago Aparicio<sup>a,\*</sup>

<sup>a</sup> Department of Chemistry, University of Burgos, 09001 Burgos, Spain

<sup>b</sup> Department of Chemical and Paper Engineering, Western Michigan University, Kalamazoo, MI 49008-5462, USA

## ARTICLE INFO

### Article history:

Received 10 March 2021

Revised 9 June 2021

Accepted 15 June 2021

Available online 17 June 2021

### Keywords:

Water

Liquid state confinement

Deep eutectic solvents

Molecular dynamics

Hydrogen bonding

## ABSTRACT

The nanoscopic properties of highly diluted water solutions in choline chloride + lactic acid deep eutectic solvent was studied using molecular dynamics simulations as a function of concentration and temperature with the objective of characterize the confinement of water in deep eutectic solvents as a non-regular confinement mechanism. The simulations allowed the analysis of changes in the properties of the deep eutectic solvent in response to the water presence as well as the behaviour of confined water in solvent cavities. The analysis of structural, energetic and dynamic factors provides for the first time the characterization of water confined in these environmentally friendly solvents. The results showed how water can be confined in deep eutectic solvents liquid cages maintaining water individuality with minor changes in the solvent properties, which can be used for tuning water properties for the development of technological applications.

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## 1. Introduction

Deep eutectic solvents (DESs) are a group of fluids which have attracted great attention both in academia and industry for their possible technological applications [1–3] into a sustainable chemistry framework [4]. Many DES are highly hygroscopic fluids [5], which hinders their application under strictly dried conditions for real industrial applications. Although this may be a disadvantage for certain application for which drying is required such as catalysis, the use of water for tailoring DESs properties to facilitate certain technological applications have also been considered [6], thus water modulates DESs physicochemical properties [7].

The effect of water on the DESs properties of DESs have been analysed in the literature [8] considering the large dependence on the extension of hydration, thus evolving from water in DESs to DESs in water solutions with increasing water content [9], leading to an unusual transition from ionic mixtures to water solutions. Therefore, in the case of large water content, electrolyte solutions in water are inferred whereas for low water content the fluids' structuring is developed through water to DES and water to water interactions, with the extension and nature of each type of interaction being also dependent on the water content [10]. Likewise, the

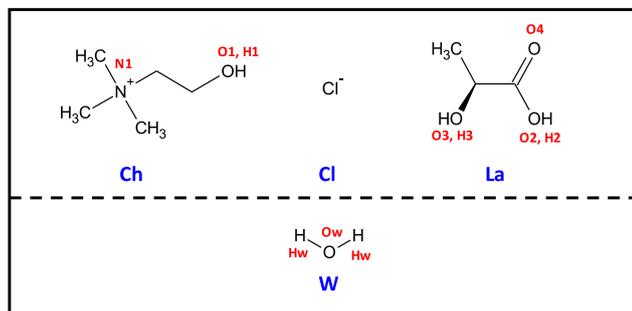
thermophysical properties of DESs are largely affected by the water content and allow fine tuning of targeted properties with the addition of controlled amounts of water. Such adjustments might lead to reduction of unsuitable DESs properties such as large viscosity values [11,12], controlling melting point [13,14] and allowing the possible scale-ups to real industrial applications.

In the case of very low water content, the behaviour of water molecules can be considered as a case of confinement in the prevailing DESs environment. The confinement of water in liquids has been previously experimentally studied for ionic liquids (ILs) [15,16], which are closely related fluids systems to DESs, showing the formation of guest (water) – host (IL) cages. The case of water in DESs have been proposed for relevant applications such as new electrolytes for batteries [17], thus the understanding of water in DESs systems at very low water content is relevant not only for basic research purposes but also for practical uses. This new type of water confinement in liquid state, herein considered as DESs, provides new avenues for modifying and controlling the properties both of the confined water and the effect of the traces of water on the DESs properties.

In this work we have considered a natural DESs (NADES), choline chloride (ChCl) : lactic acid (La) for 1:1 composition, Fig. 1, and the properties of water solutions in ChCl:La being studied using molecular dynamics (MD) simulations for low water concentrations (roughly 0 to 3000 ppm). The properties of the DES were studied as a function of the degree of hydration as well as the

\* Corresponding authors.

E-mail addresses: [mert.atilhan@wmich.edu](mailto:mert.atilhan@wmich.edu) (M. Atilhan), [sapar@ubu.es](mailto:sapar@ubu.es) (S. Aparicio).



**Fig. 1.** Structures of the molecules considered in this work for the study of ChCl:La (1:1) + W mixtures. Atom and molecular labelling used along this work is indicated in red and blue labels, respectively.

**Table 1**  
Systems used for MD simulations.

label	N(Ch)	N(Cl)	N(La)	N(W)	W content / ppm
mix_00	250	250	250	0	0
mix_01	250	250	250	1	314
mix_02	250	250	250	2	627
mix_04	250	250	250	4	1254
mix_06	250	250	250	6	1879
mix_08	250	250	250	8	2504
mix_10	250	250	250	10	3128

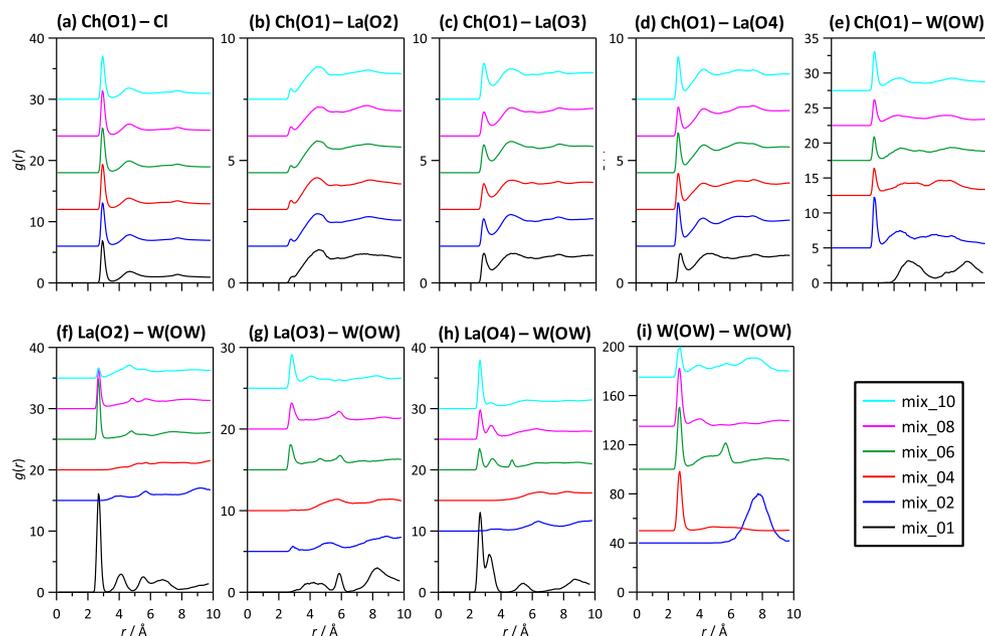
nature of hydrogen bonding. This DESs was previously studied by our group considering water contents up to 22 wt% [18] but water in DESs solutions at low water content were not previously considered. This study provides for the first time a nanoscopic characterization of the behaviour of water confined in DESs (water – in – DESs systems) as well as the effect of low water content on DES properties, which is of great relevance for DESs technological applications considering the hydrophilicity of many DESs and the costs and difficulties to obtain and work with ultra dried DESs at industrial scale.

## 2. Methods

MD simulations for ChCl:La(1:1) + water mixtures were carried out for the systems and water contents reported in Table 1, which are designed to mimic very low water content mixtures to study water confined in the considered DES. All simulations were carried out with MDynaMix v.5.2 program [19] whereas data analysis and visualization were done with VMD [20] and TRAVIS [21] codes. The force field parameterization considered for ChCl:LA modelling was reported and validated in a previous work [18] (Supplementary Information). Water molecules were described according to the SPC-E force field [22]. Initial cubic simulation boxes, with the number of molecules reported in Table 1, were built with the Packmol program [23] considering  $1 \text{ g cm}^{-3}$  initial density. Simulations were carried out in a two steps procedure: i) 10 ns simulations in the NVT ensemble for equilibration purposes at the target temperature, then followed by ii) 90 ns simulations in the NPT ensemble at the selected temperature and 1 bar for production purposes. MD was carried out for 298, 308 and 358 K for all the considered mixtures. The pressure and temperature were controlled with the Nose-Hoover method. Electrostatic interactions were treated according to the Ewald summation method [24] (15 Å for cut-off radius). Cross – terms for Lennard-Jones contributions were calculated with Lorentz-Berthelot mixing rules. The equations of motion were solved with the Tuckerman-Berne double time step algorithm [25] (1 and 0.1 fs for long- and short-time steps).

## 3. Results

The solutions studied in this work using MD simulations, Table 1, correspond to low water content (0 to 3128 ppm), thus they allow to analyze the changes in ChCl:La properties for low degrees of hydration as well as the behavior of (isolated) water molecules surrounded by the DES polar environment. The structuring of the considered mixtures was firstly analyzed by using radial distribution functions, RDFs, for selected atomic sites, Fig. 2. The DES component (Ch, Cl and La) have relevant sites, as shown in Fig. 1, to develop hydrogen bonds between them as well as with the confined water molecules. RDFs for these sites are reported



**Fig. 2.** Site-site radial distribution functions,  $g(r)$ , for the reported atomic pairs in ChCl:La (1:1) + W mixtures at different W content and 298 K.

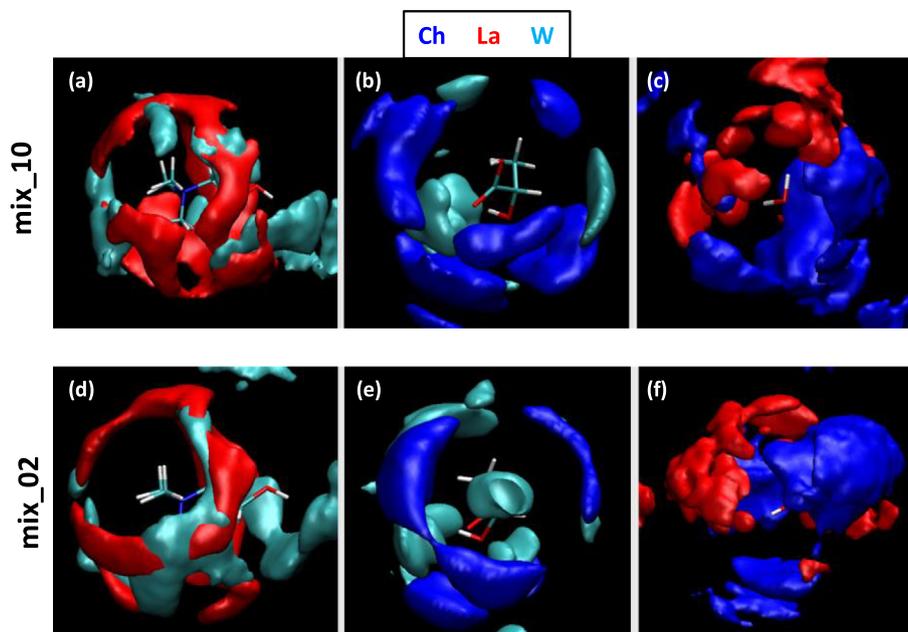


Fig. 3. Spatial distribution functions around central molecules in ChCl:La (1:1) + W mixtures at different W content and 298 K.

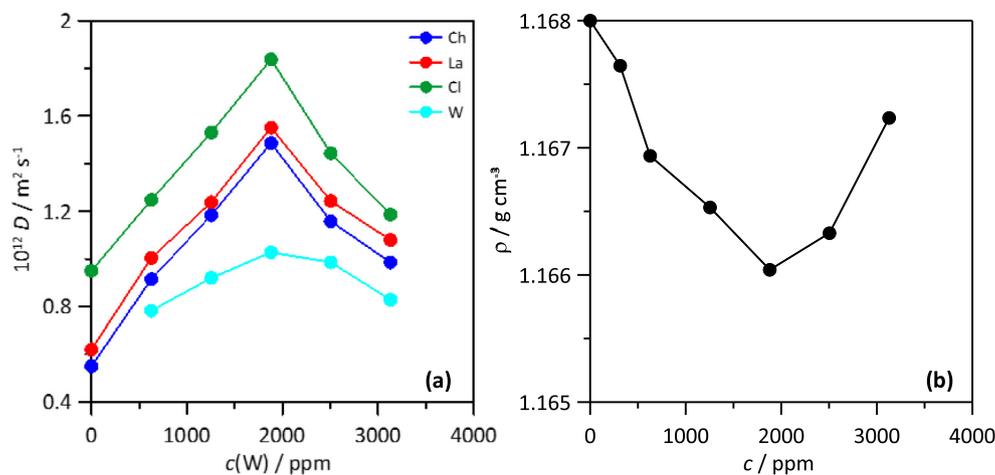
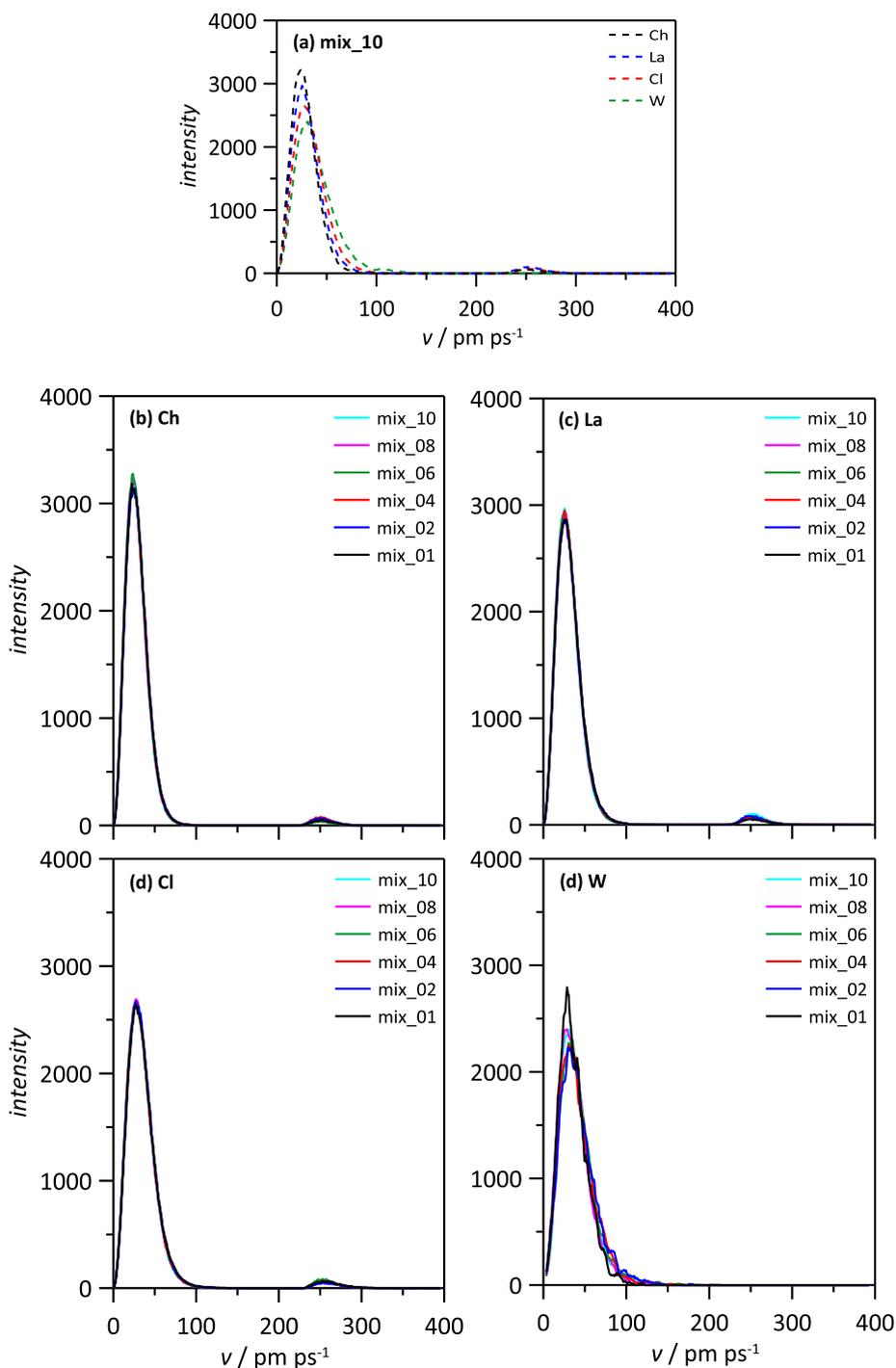


Fig. 4. (a) Self-diffusion coefficients,  $D$ , for each type of molecule and (b) density,  $\rho$ , in ChCl:La (1:1) + W mixtures at different W content and 298 K.

in Fig. 2. The Ch cation may interact through the hydroxyl site (O1, H1, Fig. 1) with Cl anion and with La molecules. The RDFs for Ch (O1) – Cl interactions, Fig. 2a, are characterized by a first peak at 2.95 Å followed by a second weaker peak at 4.6 Å, which confirm the development of cation – anion interactions through the Ch hydroxyl site. The position and intensities of RDFs peaks for Ch (O1) – Cl interactions are not affected by the presence of water molecules in the studied concentration range, thus confirming that water does not change the cation – anion interaction and it does not show disruption effect at the mentioned concentrations. Regarding the hydrogen bond acceptor (HBA; ChCl) – hydrogen bond donor (HBD; La) interactions, it should be considered that La molecules have three different sites which are prone to develop hydrogen bonds (O2, O3 and O4 sites, Fig. 1), thus the possible interaction of Ch with these three sites was considered, Fig. 2b to 2d. These results show that Ch – La hydrogen bonding is developed through O3 and O4 sites, with almost negligible interactions through O2 site, which would be occupied by La – Cl hydrogen bonding. This mechanism of Ch – La interactions is maintained also

for the studied water concentration range. Therefore, these RDFs points to the almost negligible effect of water content on the structuring of ChCl:La, with nanoscopic arrangements not dependent on the water molecules, thus pointing to the DES being able to fit (confine) water molecules maintaining its hydrogen bonding self-aggregation. Regarding the aggregation around water molecules, results in Fig. 2e show a RDF first peak at 2.7 Å corresponding to the hydrogen bonding between water molecules and the hydroxyl site (O1) in the cation. This Ch – water hydrogen bonding is present for all the concentrations with the exception of mix\_01 (a single water molecule) for which no Ch – water interaction is inferred thus showing a lower limit for developing effective interactions. In the case of La – water possible interactions, results in Fig. 2f–h show a different behavior for highly diluted solutions (mix\_01) for which hydrogen bonding with oxygen atoms in COOH group (O2 and O4 sites is inferred) whereas for the O3 site no hydrogen bonding is inferred. The increasing water content leads to hydrogen bonding with all La sites but for mix\_02 and mix\_04 no hydrogen bonding is inferred. In the case if water self – association,



**Fig. 5.** Velocity,  $v$ , distribution functions in ChCl:La (1:1) + W mixtures at different W content and 298 K. Results in panel a are obtained for mix\_10, results in panels b to e are obtained for mix\_01 to mix\_10.

Fig. 2i, it is discarded for very low water content, mix\_01 and mix\_02, but for the remaining higher concentrations water molecules show trend to interact as inferred from the RDF peaks at 2.7 Å. Therefore, purely confined water monomers can be considered only for mix\_01 and mix\_02 concentrations (314 and 627 ppm, respectively) whereas for higher concentrations the confined species should be larger water aggregates.

The spatial distribution around the DES molecules is reported in Fig. 3 for lowest and highest water content. Considering a central Ch molecule, Fig. 3a and 3d, the reported results show how water

molecules are distributed around all the cation molecule despite the existence of large concentration of cation hydroxyl group in the vicinity, especially at higher water contents. Likewise, the presence of water molecules has effect on the distribution of La molecules around the Ch cation. In the case of La, Fig. 3b and 3e, although water molecules are distributed also around the La molecule, there is a concentration in the vicinity of the hydrogen bonding sites, with minor effect because of the water content. The distribution around water molecules, Fig. 3c and 3f, clearly shows heterogeneous distribution of Ch and La molecules occupying

different spatial regions with the slightly higher Ch domination and being maintained in the studied low water content concentration range.

The presence of water molecules in the studied DES although considering highly dilutes solutions should affect the main physicochemical properties of ChCl:La. Results in Fig. 4a show the predicted self-diffusion coefficients,  $D$ , for all the involved molecules as a function of water concentration. The reported  $D$  values are in the order  $Cl > La > Ch > W$ , which is maintained in the full composition range. The low  $D$  values for water molecules indicate that water molecules are trapped in the DES hydrogen bonding network, therefore it probes the confinement of water molecules in the studied solvent. Likewise, the evolution of  $D$  with composition is non-linear with maxima at roughly 2000 ppm. The molecular mobility is lower for low water content, i.e. water monomers are trapped in the DES liquid structure with minor effect of water molecules on DES self-interactions. As the water content increases two different effects are present: i) up to 2000 ppm the size of water clusters confined into the DES structure increases (as inferred from the self-association in Fig. 2i) which increases the disruption of DES self-association, i.e. larger molecular mobility, ii) for water content larger than 2000 ppm the decrease in molecular mobility may rise from larger clusters of water confined into DES cages, with a decrease in the mobility of water molecules as well as for DES components because of the new DES – water hydrogen bonding, Fig. 2. The behavior of density in Fig. 4b, although showing negligibly small changes in density upon water addition, shows a non-linear trend with a minimum at roughly 2000 ppm that is in parallel to the  $D$  behavior, Fig. 4a. The increase of confined water clusters sizes decrease density because of their (minor) perturbative effect on DES structuring whereas beyond 2000 ppm the water – DES heteroassociation (slightly) increases density.

The dynamic properties of the studied mixtures were also analyzed considering velocity distribution functions. These distribution functions show first maxima in the 25 to 30  $\text{pm ps}^{-1}$  for the four involved species, the main difference in the distributions stands on the intensity and width of these first peaks which follow the distinct ordering (for peaks intensity)  $Ch > La > Cl > \text{water}$ , Fig. 5a. Therefore, the molecular mobility for all the involved molecules is highly correlated because of water molecules trapped in DES cages, i.e. water molecules displacements evolve with the movement of molecules in DES for the development of suitable holes into the liquid to fit the confined water molecules. The effect of water concentration on the velocity distribution functions, Fig. 5b to 5d, is almost negligible in the studied concentration range, thus the mechanism of diffusion is maintained even considering the trend of water molecules to self-aggregate, i.e. water monomers and larger aggregates confined into the DES structuring moves according to the same mechanism, which can be justified considering the small size of the considered water aggregates.

The properties of the studied solutions are also studied considering the energy of the developed intermolecular interactions for the involved molecular pairs, Fig. 6. The results in Fig. 6 show non – linear evolution for all the considered interactions, evolving through maxima of minima at roughly 2000 ppm, in agreement with results in Fig. 4. Regarding the effect of water on energies for DES self-interactions, mainly Ch-Cl and Ch-La (Fig. 6a and 6b), the variations in energy are minor, for the case of Ch – Cl a 1.4% increase (in absolute value) is inferred on going to 2000 ppm water content whereas for Ch – La a 3.1% decrease is inferred in the same water concentration range. Therefore, the studied low water content systems does not disrupt DES self-interactions remarkably. The confined water molecules allow DES component to develop self-hydrogen bonding in a similar way to neat DES. Nevertheless,

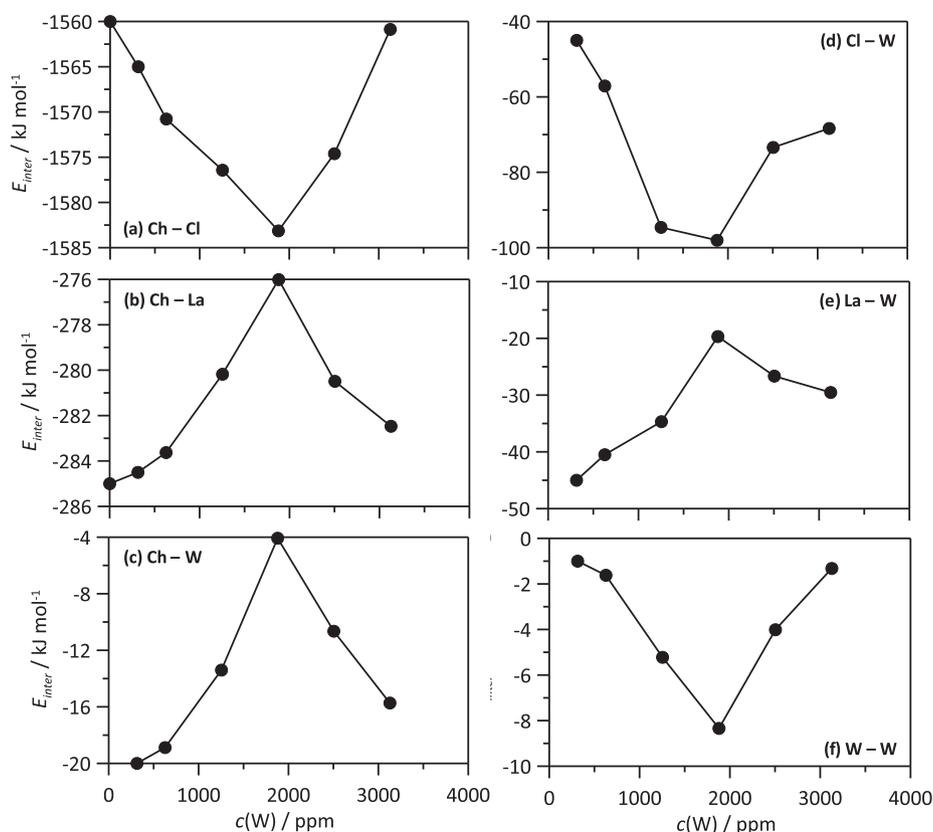


Fig. 6. Intermolecular interaction energy,  $E_{inter}$  (sum of Lennard-Jones and coulombic contributions), for each type of interacting pairs in ChCl:La (1:1) + W mixtures at different W content and 298 K.

the minor changes in Fig. 5 for density and mainly for self-diffusion should be produced by the development of DES – water interactions. The corresponding values for Ch – water, Fig. 6c, and La – water, Fig. 6e, are remarkably lower than those for Cl – La, Fig. 6d, thus showing water molecules interacting with the chlorine anion. Moreover, with the increase of water content up to 2000 ppm the anion – water interaction is reinforced, whereas the energies for Ch-water and La-water are weakened. Therefore, for monomers or small water clusters, water molecules largely interact with chlorine anion and in minor extension with Ch and La, but when water concentration increases beyond 2000 ppm although water interactions with the anion prevail, the increase of the water clusters sizes leads to a reinforcement of interactions with the Ch cation and La. The case of water-water interactions, Fig. 6f, an increase (in absolute value) of the energy up to

2000 ppm agrees with the increase in water clusters sizes, Fig. 2i, whereas going beyond that concentration decreases the water-water interaction because the water clusters start to efficiently interact with the surrounding solvent through hydrogen bonding without increasing the size of the confined water clusters.

The properties reported in previous paragraphs are originated because of the ability of developing hydrogen bonds for all the studied molecules, and thus because of the changes in these hydrogen bonding upon addition of low amounts of water. For this purpose, the number of hydrogen bonds per molecule were calculated and reported in Fig. 7 for the most relevant interaction sites. The criteria for defining hydrogen bonds was a geometrical one considering 3.5 Å and 60° for the separation of donor to acceptor (oxygen to hydrogen) and the corresponding angle, respectively. The results reported in Fig. 7 shows again a non-linear evolution with extreme

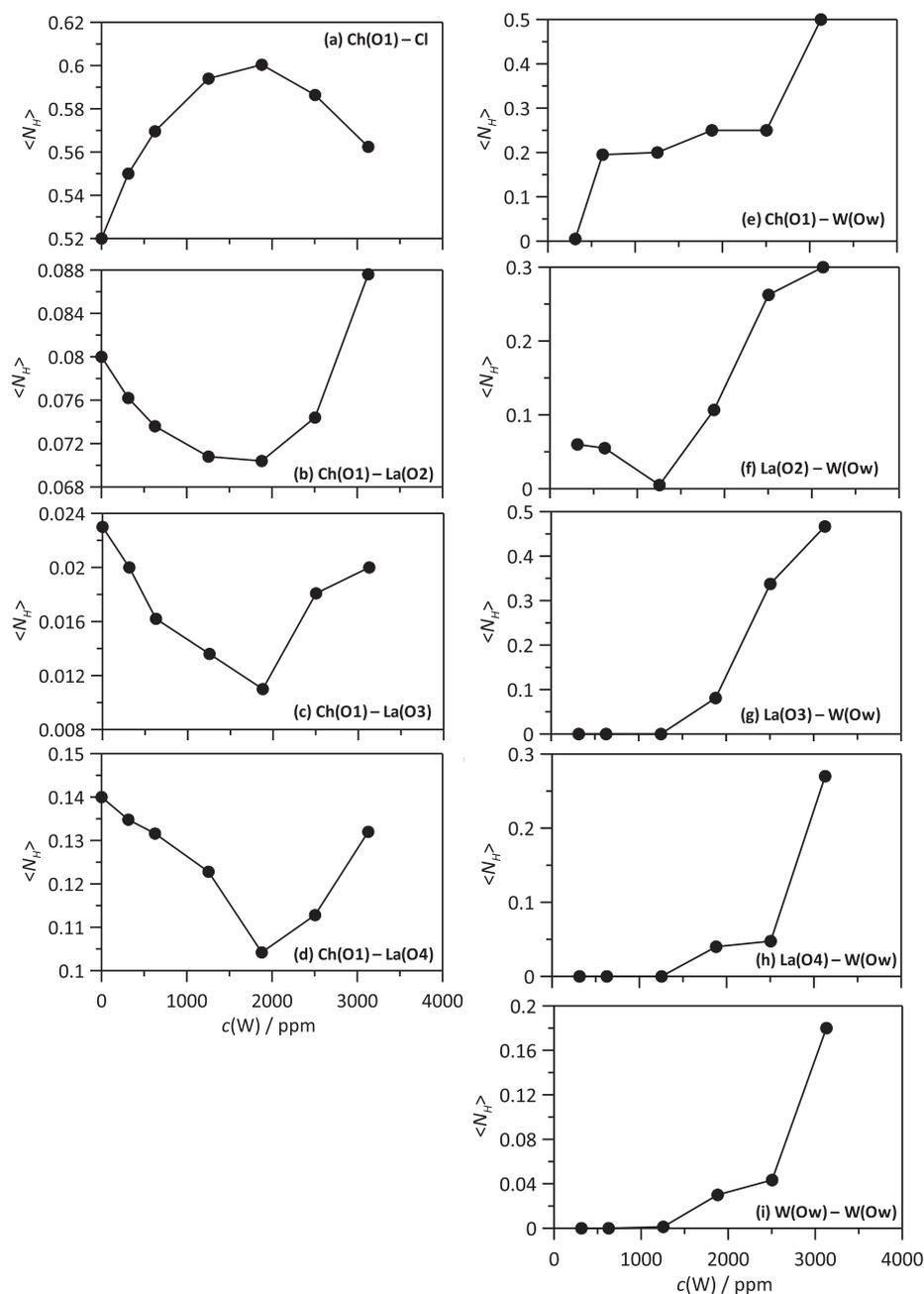


Fig. 7. Average number of hydrogen bonds,  $\langle N_{H_f} \rangle$ , (a to e) per Ch, (f to h) per La, or (i) per W molecule, for the reported sites in ChCl:La (1:1) + W mixtures at different W content and 298 K.

at roughly 2000 ppm water content for most of the cases. The number of Ch-Cl hydrogen bonds increases on going to 2000 ppm water content, which agrees with the increase of energy reported in Fig. 6b. On the contrary, the number of hydrogen bonds for all the Ch - La pairs (Fig. 7b-d) decreases, in agreement with the energy behavior in Fig. 6b. Nevertheless, the changes in the number of hydrogen bonds for DES components is minor, thus showing minor disruptive effect of water molecules. For the DES - water hydrogen bonding, results in Fig. 6e-h show almost negligible hydrogen bonding for low water content, with highly diluted solutions mainly being hydrogen bonded with Ch cation, Fig. 7e, and only when water concentration increases beyond 2000 ppm hydrogen bonding with La is not negligible. Analogous results are inferred for water - water self-hydrogen bonding, Fig. 7i, with only self-association being inferred for larger water contents, thus

allowing to confirm that for low water contents mostly water monomers are confined into the DES.

The kinetics of the formation and breaking of the developed hydrogen bonds was analyzed considering the reactive flux correlation function [26], from which the forward lifetime,  $\tau_f$ , are inferred and considered as a measurement of the hydrogen bonds lifetime, Fig. 8. As in the case of the properties reported in previous sections, the evolution of  $\tau_f$  with water content is non-linear with changes around 2000 ppm. All the  $\tau_f$  involving DES self-hydrogen bonding decrease up to 2000 ppm water content and then increase, both for Ch-Cl and Ch-La, thus although the presence of water increases the number of some types of hydrogen bonds, such as Ch - Cl (Fig. 7a), these hydrogen bonds are more dynamics (i.e. lower life times), e.g. in the case of Ch - Cl  $\tau_f$  decreases roughly 50% on going from neat DES to 2000 ppm water content, Fig. 8a,

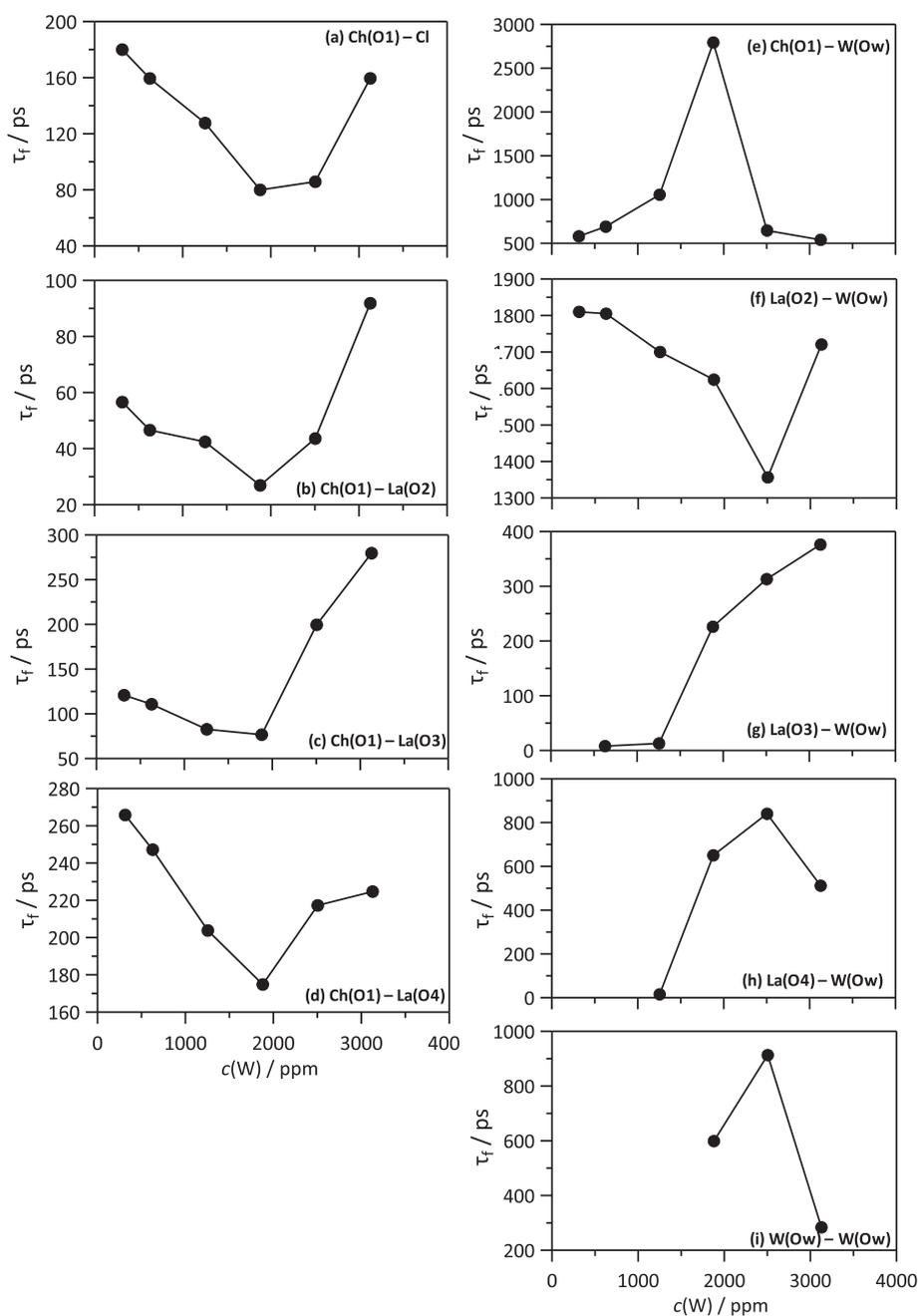


Fig. 8. Living time of hydrogen bonds,  $\tau_f$ , for the reported sites in ChCl:La (1:1) + W mixtures at different W content and 298 K.

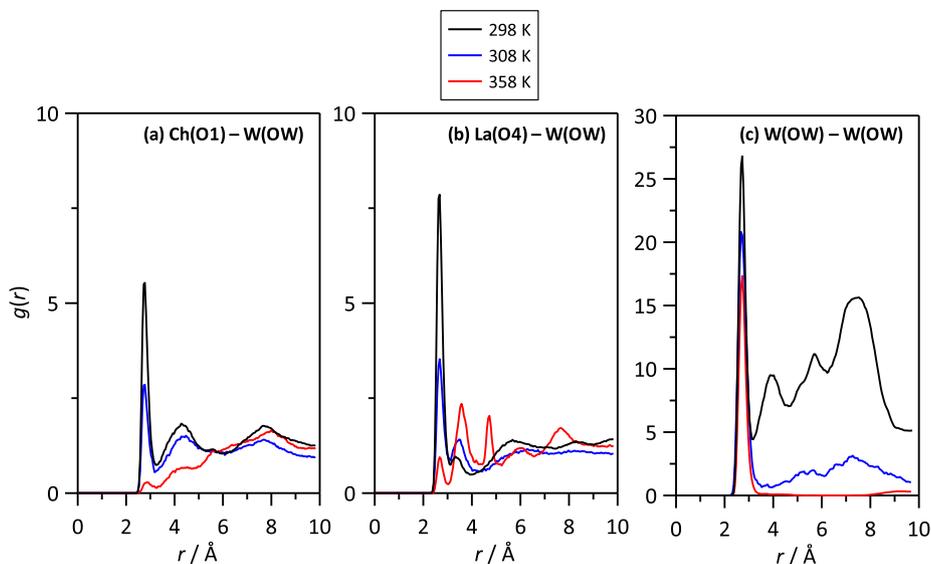


Fig. 9. Site-site radial distribution functions,  $g(r)$ , for the reported atomic pairs in ChCl:La (1:1) + W mix<sub>10</sub> at different temperatures.

although when water content increases beyond this limit  $\tau_f$  goes back to a value similar to that in neat DES, with analogous results (Fig. 8b to 8d) with for these interaction hydrogen bonds with even large lifetimes than in neat DES being inferred for the larger water content. In the case of DES – water interactions, Fig. 8e–h, larger  $\tau_f$  values have been observed in comparison to HBA and HBD cases. In the case of water-water interactions, Fig. 8i, the results do not allow to infer a clear conclusion, with these hydrogen bonds having lifetimes in the range of DES-water ones. Therefore, hydrogen bonds involving water molecules have larger lifetimes than interactions between DES components, thus showing a heterogeneity in the kinetics of hydrogen bonds, with those involving water surviving when DES-DES ones have been broken.

The effect of temperature in the properties of the studied systems was analyzed in the 298 to 358 K range. The RDFs corresponding to the interactions with water molecules are reported in Fig. 9. For Ch-water and La-water interactions, the heating up to 358 K almost vanishes the first RDF peak corresponding to the development of hydrogen bonds, thus the DES – water interactions are weakened upon heating. In the case of water-water interactions, although heating decreases the intensity of RDF peaks, Fig. 9c, this effect is remarkably lower than for DES-water interactions, Fig. 9a and 9b, thus showing that water self-association is less sensitive to DES-water ones to weakening upon heating. Therefore, confined water clusters are still self-associated at high

temperature but the interaction with the surrounding DES solvent is clearly weakened. The dynamics of the fluids with temperature was considered with velocity distribution function in Fig. 10. In all the cases heating supposes a widening of the distribution functions as the molecules have more kinetic energy upon heating and because of the decrease of water – DES interactions, which favors molecular mobility at higher temperatures. Therefore, confined water molecules in DES at high temperatures have a completely different behavior to that in close to ambient conditions, which should be considered for practical application of these solutions.

#### 4. Conclusions

The properties of water confined in choline chloride + lactic acid deep eutectic solvent was analysed as a function of water content and temperature using molecular dynamics simulations. The reported results confirm the existence of two different concentration regions, lower and higher than 2000 ppm water content, with different behaviour but in all the cases with water aggregates confined into the DES liquid structure. For low water content, water monomers are confined into the DES voids, interacting with the surrounding solvent through hydrogen bonding without largely disrupting the solvent structural properties but increasing the molecular mobility and decreasing the lifetimes of the hydrogen bonds. For larger concentrations, the disruptive effect of water

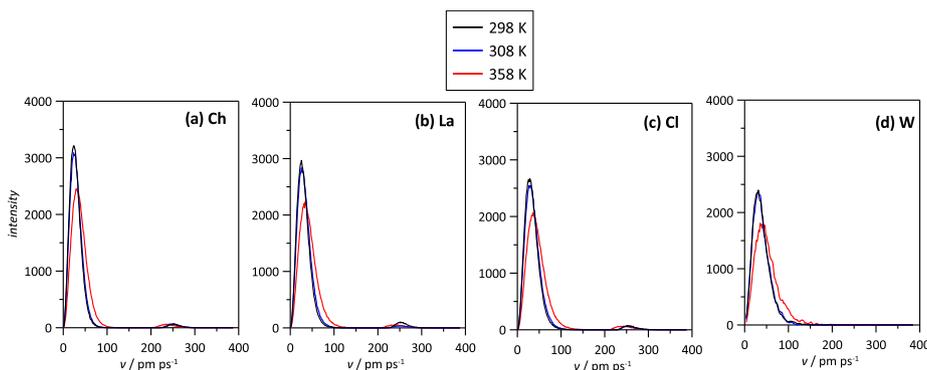


Fig. 10. Velocity,  $v$ , distribution functions in ChCl:La (1:1) + W mix<sub>10</sub> at different temperatures.

molecules is larger, because of the formation of water aggregates affecting, although in a minor extension, the DES structuring. The temperature has a large effect on the solutions properties, with large disruptive effect on water – DES interactions. The reported results show how water molecules can be efficiently confined in DES with minor changes in the solvent properties, thus for low water concentration the presence of isolated water clusters in the solvent provides a new way to have water molecules in matrix suitable for different practical application into sustainable solvent.

### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Acknowledgement

This work was funded Ministerio de Ciencia, Innovación y Universidades (Spain, project RTI2018-101987-B-I00). We acknowledge SCAYLE (Supercomputación Castilla y León, Spain) for providing supercomputing facilities. The statements made herein are solely the responsibility of the authors. Authors declare no competing interests.

### Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.molliq.2021.116758>.

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